

***Remarks***

Reconsideration of this Application is respectfully requested. Claims 1, 3-8, 14-19, 36-37, 59, 61-64, and 70-75 are active in the application, with claims 1 and 59 being the independent claims.

Applicants reserve the right to file one or more continuation or divisional applications directed to the canceled subject matter.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***The Withdrawal of the Previous Objection and Rejection***

Applicants note, with thanks, the withdrawal of the previous objection to claims 14, 15, 63, 70 and 71. Applicants also note, with thanks, the withdrawal of the rejection of the claims under 112, first paragraph, for written description and enablement.

***The Rejection Under 35 U.S.C. § 112, second paragraph***

At office action page 2, claims 15 and 71 are rejected under 35 U.S.C. § 112, second paragraph, as failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants respectfully traverse this rejection.

The Examiner notes that claims 15 and 71 refer to RGD peptide but that the claims from which claims 15 and 71 depend, claims 1 and 59, respectively, do not recite RGD peptide.

Applicants have amended claims 1 and 59 to refer to RGD peptide. Accordingly, this rejection can be withdrawn.

***The Rejection Under 35 U.S.C. § 102(b)***

At office action page 3, claims 1, 3, 4, 7, 8, 16-18, 37, 59, 63, 64 and 72-74 are rejected under 35 U.S.C. § 102(b) as being anticipated by Harris-White *et al.*, *The Journal of Neurosci.* 18: 10366-10374 (1998) (hereinafter "Harris-White") as evidenced by Sabo *et al.* *Neuroscience Lett.* 184: 25-28 (1995). Applicants respectfully traverse this rejection.

The Examiner notes that Applicants stated they canceled amyloid- $\beta$  but that the claims were then amended to still refer to  $\beta$ -amyloid. Applicants regret this error and thank the Examiner for drawing Applicants' attention to this. Claims 1 and 59 have been amended to delete  $\beta$ -amyloid. Therefore, this rejection is overcome and may be withdrawn.

***The First Rejection Under 35 U.S.C. § 103(a)***

At office action page 4, claims 1, 5, 6, 36, 59, 61 and 62 are rejected under 35 U.S.C. § 103 (a) as being unpatentable over Harris-White as evidenced by Sabo in view of Matter *et al.*, *J. Cell Biology* 141:1019-1030 (1998) (hereinafter "Matter"). Applicants respectfully traverse this rejection.

Applicants have amended the independent claims so that they do not recite  $\beta$ -amyloid. Harris-White, even in combination with Matter, does not teach or suggest exposing brain cells to an integrin antagonist as recited in the claims as currently amended, and determining the effect of a substance on the ability of the antagonist to

have its effect on the sequestration, uptake or accumulation of amyloid as recited in the claimed methods. Accordingly, *prima facie* obviousness is not established and this rejection may be withdrawn.

***The Second Rejection Under 35 U.S.C. § 103(a)***

At office action page 5, claims 1, 14, 15, 59, 70 and 71 under 35 U.S.C. § 103(a) as being unpatentable over Harris-White as evidenced by Sabo in view of Matter. Applicants respectfully traverse this rejection.

Harris-White is relied on as above. Matter is relied on as teaching a method in which DNA sequences encoding integrin  $\alpha 5$  are the "substance" and amyloid- $\beta$ , anti-integrin  $\alpha 5$  antibody and GRGDSP peptides are the "integrin antagonists." Applicants respectfully disagree.

Applicants have amended the independent claims so that they do not recite  $\beta$ -amyloid. Accordingly, Matter does not cure the deficiencies of Harris-White. Accordingly, *prima facie* obviousness is not established and this rejection may be withdrawn.

***The Third Rejection Under 35 U.S.C. § 103(a)***

At office action page 7, claims 1, 19, 59 and 75 under 35 U.S.C. 103(a) as being unpatentable over Harris-White as evidenced by Sabo, in view of Haß (Hass) *et al.*, *J. Biol. Chem.* 273:13892-13897 (1998) (hereinafter "Hass"). Harris-White is discussed above. Haas is relied upon as disclosing protein-protein interactions between amyloid- $\beta$  precursor protein APP and apoE2, apoE3 and apoE4 and as recognizing that the apoE4

isoform is associated with development of Alzheimer's disease and is considered a susceptibility factor for Alzheimer's disease. Applicants respectfully traverse this rejection.

Applicants have amended the independent claims so that they do not recite  $\beta$ -amyloid. Harris-White is discussed above. Hass does not cure the deficiencies of Harris-White. Accordingly, *prima facie* obviousness is not established and this rejection may be withdrawn.

### ***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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